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EXAMINER	
ZEMAN, MARY K	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/028,018	ERLANDER ET AL.	
	Examiner	Art Unit	
	Mary K Zeman	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4 and 7-32* is/are pending in the application.

4a) Of the above claim(s) *1,3,4,7-14 and 22-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-21 and 30-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,3,4 and 7-32* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3, 4, 7-32 are pending in this application. Claims 2, 5 and 6 have been canceled. Claims 30-32 are newly added.

Applicant's election with traverse of Group V in Paper No. 11/26/03 is acknowledged. The traversal is on the ground(s) that Groups V and VI are related as they both use the same types of sequences to stage breast cancer, and the inventions are classified in the same subclass. This is not found persuasive because the independent claims do not use the same types of genes. Claim 15 utilizes genes that correlate with stages of breast cancer, while claim 22 utilizes genes that discriminate between stages of breast cancer. These are not necessarily the same classes of genes. While some types of genes may belong to both classes, the classes do not completely overlap, and the criteria for each class is different.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1, 3, 4, 7-14, and 22-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11/26/03.

Claims 15-21 and 30-32 are under examination.

Information Disclosure Statement

The information disclosure statements filed 7/1/02, 4/21/03, 9/2/03 and 11/26/03 have each been entered and considered. Initialed copies of the PTO-1449 forms are included with this action.

Claim Objections

Claim 19 is objected to as it depends from a withdrawn claim. Claim 19 should be amended to recite the appropriate products or properties recited in Claim 1.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. See for example, p27.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection. The claims are drawn to methods of determining the stage of breast cancer of a sample by assaying "one or more genes correlated with one or more stages of breast cancer." Claims 15-18, 20 and 21 are not limited to any particular sequences, and claim 19 is limited to genes disclosed in Tables 2-5.

The specification sets forth multiple tables. The categories of information in Tables 2-5 for each row are "CloneID" "Weight" and "Description." The CloneID is defined at page 27 as being a "IMAGE consortium Clone ID number" as references to a web site. "weight" refers to an absolute value of a difference in expression between samples. Description is defined as "a brief identifier of what the gene encodes." This information does not provide a written description for the claimed invention. These tables to not specifically identify the exact polynucleotide sequences that are correlated with breast cancer, nor do they reference a stable, known and non-changing source of information. The webpage cited is continually updated with new information. There is no sequence listing correlating a listed CloneID with a particular tag useful in the correlation of expression levels in stages of breast cancer. The specification does not provide one of skill in the art with the materials in hand to perform the methods of the invention. Many of the items in the tables are described only as "ESTs" which is an acronym for

"Expressed Sequence Tag", a non-specific acronym. Others have descriptions of an activity, or homologous sequence, but not an identification of the sequence itself. Even if a fairly specific gene name is listed, it is unclear what portion of the gene sequences was used, or is suitable for use in the claimed methods. It is unclear if *any* subsequence of the referenced gene is useful and correlated with a particular stage of breast cancer.

Even if the reference to the webpage could provide information leading to identification of the sequences required to perform the claimed method, the pages themselves are insufficient. The Examiner reviewed the referenced webpage/ site. In the Frequently Asked Question portion (Printout attached), the IMAGE Consortium notes that sequences can be removed from the database that had previously been referenced. This is a removal of information material to the performance of the claimed methods. These pages also address confusion as to what all the accession numbers, CloneID numbers and GI numbers actually reference. Also issues regarding sequences in other databases that recite a CloneID that are not in the IMAGE database are discussed.

In regards to the claims which do not reference the Tables, there is a lack of guidance in the specification as to what exactly characterizes or identifies "a gene correlated with one or more stages of breast cancer". No particular characteristics of the sequences are set forth such that a genus of structures could be considered to have been disclosed. The identification of a sequence by its activity alone is not a description of the sequence itself. The claims encompass a genus of compounds defined only by their function wherein the relationship between the structural features of the members of the genus and said function have not been defined. In the absence of such a relationship either disclosed in the as-filed application or which would have been recognized based upon information readily available to one skilled in the art, the skilled artisan would not know how to make and use compounds that lack structural definition. The fact that one could have assayed a compound of interest using the claimed assays does not overcome this defect since one would have no knowledge beforehand as to whether or not any given compound (other than those that might be particularly disclosed in an application) would fall within the scope of what is claimed. It would require undue experimentation (be an undue burden) to randomly screen undefined compounds for the claimed activity.

All of these problems illustrate the problem of identifying exactly what is to be used in the methods of the invention, and the lack of a written description of those materials in the specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-21 and 30-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The metes and bounds of the limitations of claim 15 are unclear. The method does not set forth steps to actually determine the stage of a breast cancer sample. The claim merely assays for expression for one or more genes. The genes can be correlated to one or more stages of cancer. If the expression of the one or more genes is correlated with more than one stage of breast cancer, the goal is not accomplished. There is no step of analyzing the results of the assay and assigning a stage of breast cancer. The only step required is performing the assay. Claim 16 indicates that the assaying is only preparing the mRNA- and not actually identifying any level of expression. Claims 18-19 "use" an array, without specifically identifying how it is to be used, and correlated. Claim 20 indicates that the genes can be correlates with all of the stated stages of breast cancer. How this helps to identify the stage of cancer in a sample is unclear. Similarly, claim 21 indicates that the same genes can correlate with both normal *and* abnormal cells. The limitations of claims 30-32 do not clarify the problems with claim 15. As such, one of skill in the art would be unable to determine exactly what steps should be performed with what materials in order to meet the goal of determining the stage of breast cancer in a particular type of sample.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 15-21 and 30-32 are rejected under 35 U.S.C. 102(e) as being anticipated by Soito et al. (USP 6,673,024).

The claims are drawn to methods of determining the breast cancer stage of a ductal lavage sample comprising assaying for expression of one or more genes correlated with one or more stages of cancer. MRNA from the sample can be assayed, amplified, and tested on an array. The genes can be correlated with normal or abnormal cells, or with various stages of cancer. Multiple genes can be assessed, the sample can be from a human, and the human can be suspected of having breast cancer.

Soito et al. (USP 6,673,024) discloses methods of identifying a stage of breast cancer (normal, malignant or atypical- columns 3-4) by studying a ductal lavage sample (column 3) of a patient (human) suspected of having breast cancer, or having breast cancer. The methods of Soito et al. can include assaying for the expression of one or more genes correlated with a stage of breast cancer (column 5) Specifically disclosed markers include the estrogen receptor, EGFR, p53, HER-2 neu, CEA, PSA, ErbB2, LDH, GCDFP-15 and collections are referred to at columns 13-14. The assay can be of mRNA on an array, and multiple genes can be tested. As such, Soito anticipates the rejected claims.

Claims 15-21, and 30- 32 are rejected under 35 U.S.C. 102(e) as being anticipated by Hung (USP 6,642,009).

Hung (USP 6,642,009) discloses methods of staging a breast cancer ductal lavage sample. The lavage samples are examined to determine the presence of a marker associated with breast cancer, or pre-cancer (staging). A number of differing markers are specifically identified as markers of interest in staging breast cancer, including CEA (col 1), p53 (col 4), and G-actin (col 4), LPA (col 6), paladin (col 6) and all the markers at columns 7-9, 14-15 and claims 4 and 15. Stages of breast cancer studied by Hung include hyperplasia, ADH, LG-DCIS, HG-DCIS,

pre cancerous, normal, invasive carcinoma (column 9). mRNA from the sample can be assessed. As such, Hung anticipates the rejected claims.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary K Zeman whose telephone number is (571) 272 0723.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P Woodward can be reached on (571) 272 0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MARY K. ZEMAN
PRIMARY EXAMINER